REMARKS

Status of Claims and Amendment

Upon entry of the amendment, which is respectfully requested, claim 9 will be amended, claim 33 will be canceled, and new claims 34 and 35 are added.

Claim 9 has been amended to even further clarify that the claimed method measures the occupancy of a compound that is bound to an epitope region recognized by antibodies 45531.111 and 45523.111 of CCR5 on a CCR5 expressing cell or a membrane fraction. Also, measurement of the ability of the compound to inhibit binding of antibodies 45531.111 and 45523.111 to the epitope region is measured after 6 to 10 washings. Support for the amendment to claim 9 may be found at least at page 39, lines 22-23, page 41, lines 3-19, the paragraph bridging pages 41-42, and page 42, lines 10-26.

Support for new claims 34 and 35 may be found at least at page 41, lines 3-19.

No new matter is added.

Response To Claim Rejection under 35 U.S.C. § 112, 1st Paragraph

Claim 33 is rejected under 35 U.S.C.§112, 1st paragraph, as allegedly being non-enabled.

The Office Action states that antibodies 45531.111 and 45523.111 recited in claim 33 are essential to the claimed invention and the reproduction of antibodies from hybridomas is an extremely unpredictable event. Thus, the Office Action asserts that Applicants must demonstrate that the same antibodies are obtainable by a repeatable method set forth in the specification or otherwise readily available to the public or, in the alternative, provide a Statement of Availability in accordance with the Patent Office rules.

Claim 33 is canceled herein thereby rendering the rejection moot as to this claim.

Applicants provide the following with respect to present claims 9, 34, and 35.

Applicants respectfully submit that the 45531.111 antibody and the 45523.111 antibody are commercially available from R&D as described in the specification, for example at page 41, lines 24-26. Also, they are on sale by the following companies:

* Clone 45523.111

Santa Cruz Biotechnology Inc (Cat.No:sc-57070)
Affinity BioReagents (Cat.No:MA1-24666)
abcam (Cat.No:ab10397)
Gene Tex Inc (Cat.No:GTX10397)
Novus biologicals （Cat.No:NB120-10397)

* Clone 45531.111

Neuromics (Cat.No:MO15077).

Accordingly, the 45531.111 antibody and the 45523.111 antibody are widely available to the public, and the enablement requirement is satisfied.

In view of the above, Applicants respectfully request withdrawal of the §112, 1st paragraph rejection.

Response to Claim Rejection under 35 U.S.C. § 112, 2nd Paragraph

Claims 9 and 33 are rejected under 35 U.S.C. § 112, 2nd paragraph, as allegedly being indefinite.

Specifically, the Office Action objects to the term "strong binding site" as a relative term. The Office Action suggests deleting the word "strong" to overcome the rejection.

The Office Action also objects to the phrase, "the antibody has the property of not binding to CCR5".

Additionally, the Office Action states that the phrase "or an isotype control of the labeled anti-CCR5 antibody" is confusing.

Claim 33 is canceled herein thereby rendering the rejection as to claim 33 moot.

Claim 9 is amended herein, thereby obviating the rejection.

Also, the 45531.111 antibody or the 45523.111 antibody and its isotype control are not allowed to react at the same time. Accordingly, the isotype control does not bind to the 45531.111 antibody or the 45523.111 antibody.

In view of the above, Applicants respectfully request withdrawal of the §112, 2nd paragraph rejection.

Response to Rejections under 35 U.S.C. § 103

The Office Action maintains the rejection of claim 9 under 35 U.S.C. § 103 as allegedly being unpatentable over WO '826.

The Office Action also maintains the rejection of claim 9 under 35 U.S.C. § 103 as allegedly being unpatentable over US '625.

Without conceding the merits of the rejection, claim 9 is amended herein. As amended, the presently claimed method for measuring an occupying ratio of a receptor has the following features not taught or suggested by the cited reference.

* The compound which binds to the binding site is capable of continuously binding to the receptor. Accordingly, the compound which binds to the binding site is important.
* The epitope of the 45531.111 antibody or the 45523.111 antibody is a strong binding site of CCR5, and the antibodies are very important for measuring an occupying ratio of a compound which binds to the strong binding site.
* An antibody in which the strong binding site is not an epitope cannot be used for measuring an occupying ratio of a compound which binds to the strong binding site.

The epitope region recognized by the 45531.111 antibody or the 45523.111 antibody is a strong binding site that is essential in the claimed invention, and the compounds which bind to the epitope region is different from other compounds which bind to the binding site of the chemokine receptors. For instance, a compound that binds to the strong binding site or epitope region recognized by the 45531.111 antibody or the 45523.111 antibody, is present after stringent washing conditions because the compound cannot be easily washed off the site even after 6 to 10 washes.

Further, WO 98/18826 ("WO '826") is directed to an antibody that binds to the chemokine receptor-5 protein (CCR5) or portion of the receptor (see last paragraph of page 3 of WO '826). The antibody of WO '826 is disclosed to be specific for human CCR5, and blocks the binding of a chemokine, e.g., MIP-1α and MIP-1β, to inhibit the function associated with the binding of the chemokine (see page 4, lines 1-11 of WO '826). The antibody disclosed by WO '826 is used to competitively block or inhibit chemokine ligand binding to the chemokine binding site of CCR5 (see page 4, lines 18-25 of WO '826). In this regard, the radioligand

binding assay disclosed at pages 64-65 of WO '826 evaluates the ability of unlabeled anti-CCR5 mAb to block or inhibit the binding of radiolabeled chemokine ligands, MIP-1α and MIP-1β, to CCR5 at the chemokine receptor binding site based upon the displacement in total binding of the radiolabeled MIP-1α and MIP-1β to CCR5 by the unlabeled anti-CCR5 mAb.

In contrast, the presently claimed method measures the binding of a test compound to a strong binding site which is an epitope region of CCR5 that is recognized by the antibodies 45531.111 and 45523.111. The present invention evaluates the occupancy ratio of a test compound by its ability to block or inhibit the binding of labeled antibodies 45531.111 and 45523.111 to this epitope region.

Thus, in contrast to WO '826, which determines compound binding at the chemokine receptor binding site, the present method determines compound binding at the epitope region that recognizes the antibodies 45531.111 and 45523.111. The present invention is characterized by a method for measuring an occupying ratio of a receptor for a compound which binds to the strong binding site. The antibody suitable for measuring the occupying ratio of a receptor for a compound which binds to the strong binding site was found for the first time in the present invention. The cited references, whether alone or in combination, do not teach or suggest this feature of the present invention. For at least this reason, the present invention is not rendered obvious.

Accordingly, Applicants respectfully request withdrawal of the §103 rejections.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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